UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/888,639	06/26/2001	Randolph J. Noelle	P 0280639	9079

7278 7590 12/29/2005

DARBY & DARBY P.C.
P. O. BOX 5257
NEW YORK, NY 10150-5257

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/888,639	NOELLE ET AL	
	Examiner	Art Unit	
	Phillip Gambel	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4,7-11,13-15,17,20,21,24-26,28-31,34,35,38-40,42,43 and 46-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4,7-11,13-15,17,20,21,24-26,28-31,34,35,38-40,42,43 and 46-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office Action has been withdrawn pursuant to 37 CFR 1.114.
Applicant's submission filed on 10/3/05 has been entered.

Applicant's amendment, filed 10/3/05, has been entered.
Claims 1, 15, 30 and 42 have been amended

Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are under consideration in the instant application.

Claims 2-3, 5-6, 12, 16, 18-19, 22-23, 27, 32-33, 36-37, 41, 44-45 have been canceled previously.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 7/3/04.
The rejections of record can be found in the previous Office Actions.

3. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed.
The specification as originally filed does not provide support for the invention as now claimed:
"Administering "a donor cell which expresses at least one donor antigen and which contact-dependent helper effector function" "from five to eight days prior to transplantation of the tissue or organ".

Applicant's amendment, filed 3/2/05, provides direction to page 11, lines 6-7 and page 14, lines 30-33 of the instant specification for the amendment to the claims.

Page 11 of the instant specification provides for administering anti-gp39 antibody prior to tissue or organ transplantation (e.g. 5 – 8 days before transplantation) and
the specific Example disclosed on page 14 of the instant specification only provides for administering (C57BL x BALB/c)F_1 allogeneic spleen cells 5 – 8 days prior to islet allograft transplantation in C57BL/6J mice.

However, the claims are broader than the limited Example disclosed on page 14 of the specification as filed.

The specification as filed does not provide sufficient written description for administering "a donor cell which expresses at least one donor antigen and which contact-dependent helper effector function" "from five to eight days prior to transplantation of the tissue or organ", as currently claimed.

Applicant's reliance on possibly a single or limited species do/does not provide sufficient direction and guidance to the "limitations" currently claimed.

It is noted that a generic or a sub-generic disclosure cannot support a species unless the species is specifically described. It cannot be said that a subgenus is necessarily described by a genus encompassing it and a species upon which it reads. See In re Smith 173 USPQ 679, 683 (CCPA 1972) and MPEP 2163.05.

The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office Action.

Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above. See MPEP 714.02 and 2163.06.

5. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Lederman et al. (U.S. Patent No. 6,403,091) in view of Berschorner (U.S. Patent No. 5,597,563), Cobbold et al. (U.S. Patent No. 6,056,956) and Cornaby et al. (U.S. Patent No. 4,959,302) essentially for the reasons of record and in further view of Sachs et al. (U.S. Patent No. 6,296,846).

Applicant's arguments, filed 3/2/05, have been fully considered but are not found convincing essentially for the reasons of record set forth in the previous Office Actions.

Applicant's After Final Amendment, filed 8/3/05, was entered.

As pointed out in the Advisory Action, mailed 8/31/05, applicant's arguments and the examiner's rebuttal appear to essentially the same of record.

In addition to the examiner's rebuttal of record and reiterated herein for applicant's convenience, the following is noted.

Newly added Sachs et al. also provides for pre-conditioning regimens for the transplant regimen to occur between days –1 and –8 (e.g. see entire document, particularly column 8, paragraph 2).

Also, it is noted that where the general conditions or a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experiments. See In re Aller,105 USPQ 233, 235 (CCPA 1955).

A particular parameter must be first recognized as a result-effective variable, a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said varible might be characterized as routine experimentation. See In re Antoine, 195 USPQ 6 (CCPA 1977).

Here, the art recognized a fair amount of therapeutic discretion by the ordinary artisan at the time the invention was made in providing the appropriate dosing and scheduling to achieve graft survival and a tolerance perimissive environment. The various times including those encompassing 5-8 days prior to transplantation for conditioning of the transplant recipient are provided in the prior art.

The rejection of record including another reference to address the pre-transplant conditioning regimen time period encompassed by the claimed methods renders the claimed methods obvious for the reasons of record.

The following is of record.

Applicant argued that the prior art does not teach nor suggest the administration of tolerizing agents "from five to eight days" prior to transplantation of the tissue or organ to be transplanted, as currently amended in the instant claimed methods.

As applicant noted Berschorner teach the duration of an immunosuppressive such as cyclosporine can be administered from about 7 days to about 28 days prior to the infusion of tolerogenic APCs (e.g. see columns 8-9, overlapping paragraph).

Cobbold et al. teach immunosuppressive anti-T cell antibodies can be administered repeatedly from 1 – 7 days prior to exposure to tolerogenic antigen (e.g. see column 4, paragraph 3).

Cornaby et al. teach the adjustment of immunosuppressive therapy to combat rejection and that measurement of IL-2 or IL-2 receptor levels provide such information concerning impending rejection from 2 –8 days prior to a rejection episode. (e.g. see Detailed Description of the Invention, including column 9, paragraph 1-2) and that is can be helpful in appropriate scheduling of procedures associated with grafts (e.g. columns 9-10, overlapping paragraph).

The administration of tolerizing agents "from five to eight days" prior to transplantation appears well within the variable of an immunosuppressive regimen that achieved a recognized result of inhibiting or preventing graft rejection and of creating a tolerogenic environment in order to achieve long term graft survival and well within the purview of the ordinary artisan meeting the needs of the patient and desired outcome.

As pointed out previously, Cobbold et al. teach methods of preventing graft rejection in tissue and organ transplants with anti-T cell antibodies in order to induce tolerance by providing antigen (see entire document, including columns 1-4). Cobbold et al. teach the provision of the antigen and the immunosuppressant at different times to provide a tolerance-permissive environment (see column 1-4).

The ordinary artisan provided immunosuppression prior, during and after transplanting grafts of interest, including encompassing the newly amended regimen.

In addition, the prior art recognized monitoring impending rejection encompassed by the time frame of the newly amended regimen.

Further, it is noted that the claimed methods recite "comprising" which leaves the claim open for the inclusion of unspecified ingredients even in major amounts. See MPEP 2111.03.

As pointed out previously and in contrast to applicant's assertions and given the teachings of providing antigen and/or antigen presenting cells containing the antigen to which specific tolerance is desired, including those at the time transplant, contemporaneously with immunosuppressants, as taught by Berschorner and/or Cobbold; one of ordinary skill in the art would have been motivated to combine the immunosuppressive properties of the CD40L-specific antibodies, taught by Lederman et al., to create an environment conducive to tolerance or specific unresponsiveness in the transplantation of a number of tissues and organs at the time the invention was made.

In contrast to applicant's assertions and given the teachings of Cobbold et al. that the presence of antigen as well as the use of anti-T cell antibodies can provide an environment conducive to tolerance or specific unresponsiveness, one of ordinary skill in the art would have had a reasonable expectation of success and motivation to employ the CD40L-specific antibodies in combining antigen presenting cells in transplanting a variety of tissues and organs at the time the invention was made.

It would have obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of Berschorner AND/OR Cobbold et al. to those of Lederman et al. to provide methods of providing an environment conducive to tolerance or specific unresponsiveness by combining an immunosuppressant such as the CD40 ligand-specific antibodies, taught by Lederman et al. with a source of alloantigen or xenoantigen, as taught by Berschorner and Cobbold et al. to transplant a variety of tissues and cells. A person of ordinary skill in the art would have been motivated to produce this resultant therapeutic regimen to provide an environment conducive to tolerance or specific unresponsiveness to decrease the rejection of the transplanted tissue or organ and to increase the survival of such transplants.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

6. Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over
claims 1-34 of U.S. Patent No. 5,683,693,
claims 1-34 of U.S. Patent No. 5,902,585, and
claims 1-7 of U.S. Patent No. 6,375,950

for the reasons of record and further in view of Berschorner (U.S. Patent No. 5,597,563), Cobbold et al. (U.S. Patent No. 6,056,956), Cornaby et al. (U.S. Patent No. 4,959,302) and Sachs et al. (U.S. Patent No. 6,296,846) for the reasons set forth above in the rejection under 35 § USC 103(a).

Although the conflicting claims are not identical, they are not patentably distinct from each other because the pending claims and the patented claims appear to read on the same or nearly the same methods of inducing specific unresponsiveness. Further, the patented claims appear to anticipate the instant methods.

Applicant's arguments and the examiner rebuttal are essentially the same as set forth above in the rejection under 35 § USC 103(a).

Applicant argues that the prior art does not teach nor suggest the administration of tolerizing agents "from five to eight days" prior to transplantation of the tissue or organ to be transplanted, as currently amended in the instant claimed methods.

For the reasons above, the administration of tolerizing agents "from five to eight days" prior to transplantation appears well within the variable of an immunosuppressive regimen that achieved a recognized result of inhibiting or preventing graft rejection and of creating a tolerogenic environment in order to achieve long term graft survival and well within the purview of the ordinary artisan meeting the needs of the patient and desired outcome.

It was well known and practiced by the ordinary artisan to provide immunosuppression prior, during and after transplanting grafts of interest, including encompassing the newly amended regimen.

In addition, the prior art recognized monitoring impending rejection encompassed by the time frame of the newly amended regimen

Applicant's arguments have not been found persuasive.

Claims 1, 4, 7-11, 13-15, 17, 20-21, 24-26, 28-31, 34-35, 38-40, 42, 43 and 46-50 are directed to an invention not patentably distinct from claims 1-34 of commonly assigned U.S. Patent No. 5,683,693 and claims 1-34 of commonly assigned U.S. Patent No. 5,902,585 and further in view of Berschorner (U.S. Patent No. 5,597,563), Cobbold et al. (U.S. Patent No. 6,056,956), Cornaby et al. (U.S. Patent No. 4,959,302) and Sachs et al. (U.S. Patent No. 6,296,846) for the reasons set forth above in the rejection under 35 § USC 103(a).

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 5,683,693 and U.S. Patent No. 5,902,585, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 37 CFR 1.78(c) and 35 U.S.C. 132 to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

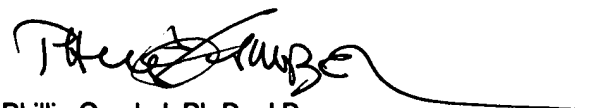
Applicant's previous amendment indicates that terminal disclaimer will be filed upon clarification of the inventorship and ownership.

7. No claim allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Phillip Gambel, Ph.D., J.D.
Primary Examiner
Technology Center 1600
December 27, 2005